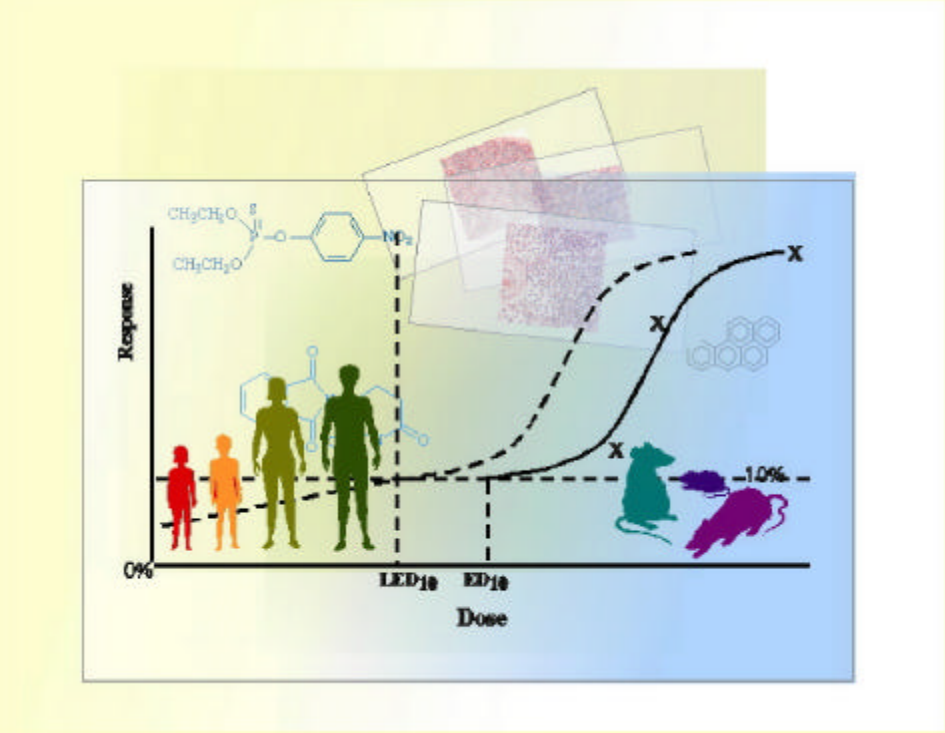
HUMAN HEALTH RISK ASSESSMENT

Oxydemeton-methyl



U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)
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HUMAN HEALTH RISK ASSESSMENT

Oxydemeton-methyl

Phase 5

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INTRODUCTION

This revised human health risk assessment for oxydemeton-methyl incorporates the most recently submitted information on the potential for adverse heritable effects, worker exposure estimates (handler and postapplication), the results of a probabilistic assessment of acute dietary exposure and risk, and a new Health Effect's Division assessment of chronic dietary exposure and risk based on an endpoint for cholinesterase inhibition in laboratory animals rather than human volunteers. In addition, this document incorporates HED's response to comments from the U.S. Department of Agriculture and Land Grant Universities regarding data requirements for alfalfa. This assessment supersedes the 12/14/98 preliminary risk assessment (made publicly available) and the 9/2/99 assessment, which incorporated the public comments received on the 12/14/98 assessment.

1.0 EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human health assessment for the active ingredient oxydemeton-methyl ((S-[2-(ethylsulfinyl)ethyl] O,O-dimethyl phosphorothioate) for the purposes of making a reregistration eligibility decision. HED evaluated the toxicological, residue chemistry, and exposure data bases for oxydemeton-methyl and determined that the data are adequate to support reregistration.

Oxydemeton-methyl is a restricted use pesticide. It is a broad spectrum, systemic organophosphate insecticide/acaricide registered for foliar and bark treatment uses to control many insects, primarily aphids, mites, and thrips. Registered use sites include terrestrial food crops (vegetable, field, tree fruit and nut crops) and terrestrial non-food crops (forestry uses). At this time, products containing oxydemeton-methyl are intended solely for use in agricultural and non-agricultural settings by occupationally employed individuals. None of the registered occupational uses are likely to involve applications to public access areas or residential sites other than soil injection by certified applicators to shade trees and ornamentals.

A Special Review of oxydemeton-methyl was initiated in 1987 (PD 1, Federal Register Vol. 52, pg. 192, 10/5/87) due to concerns over reproductive effects and worker exposure. At the time the Special Review was initiated, Miles Inc. was the basic producer of oxydemeton-methyl. On September 1993, Miles requested voluntary cancellation of all oxydemeton-methyl products, and on June 1994, Miles submitted an application to transfer all products to Gowan Company. Gowan Company signed a Settlement Agreement with the Agency in September 1994. At the time that Miles requested voluntary cancellation of its products, the due dates for data to support reregistration of oxydemeton-methyl were approaching and subsequently lapsed. Therefore, the Agency required risk mitigation concessions from Gowan to allow oxydemeton-methyl products to remain on the market while the required data were being generated. Gowan agreed not to market oxydemeton-methyl on ***citrus, field corn, popcorn, onions, pears, safflower, snap beans, sorghum, and turnips.*** *An exception to this agreement permits use of oxydemeton-methyl on citrus grown in Florida under Special Local Need (SLN No. FL960006). Also in accordance with the agreement, established tolerances were to be retained to allow these uses to be potentially reinstated after EPA's favorable review of the required data and completion of the dietary and worker risk assessments.*

The toxicological database provides consistent evidence that oxydemeton-methyl inhibits cholinesterase (ChE) in dogs, hens, humans, mice, rabbits and rats. In acute toxicity studies, oxydemeton-methyl exhibits high toxicity via the oral, dermal and inhalation routes of exposure. Inhibition of plasma, erythrocyte and brain ChE activity is dose-related and occurs by all routes of exposure and following exposure for various durations. In acute and chronic neurotoxicity studies there was no evidence of neuropathy following single and repeated doses in rats. Delayed neuropathy was observed following single, but not repeated, doses in hens.

In addition to ChE inhibition, the results of reproductive toxicity studies in the rat showed decreased male and female fertility of unknown origin. Even though oxydemeton-methyl produces reproductive toxicity, there is no indication of increased sensitivity of the offspring of rats or rabbits after prenatal and/or postnatal exposure to oxydemeton-methyl. An earlier decision to retain the 10x Food Quality Protection Act (FQPA) safety factor (as required by FQPA of August 3, 1996) based on a concern for possible adverse heritable effects (induction of somatic cell mutations in mice and evidence of DNA strand breaks in rat testes cells), was re-evaluated. Based on new toxicokinetic data, the FQPA safety factor was removed for all populations (Safety Factor Committee memorandum dated July 22, 1999).

Oxydemeton-methyl has been classified in “Group E” (i.e., the chemical is characterized as “Not Likely” to be carcinogenic in humans via relevant routes of exposure) because no compound-induced carcinogenic response was observed in mice or rats. In a metabolism study in the rat, urinary excretion was found to be the major route of elimination.

The toxicity endpoints selected for risk assessment are based primarily on neurotoxic effects of cholinesterase (ChE) inhibition in the brain, red blood cell (RBC), and plasma, as well as clinical signs (tremors). Dose levels of 2.5 mg/kg/day (single oral dose) and 0.0125 mg/kg/day (repeated oral doses) were selected for acute and chronic dietary risk assessment, respectively. Dose levels of 5.0 mg/kg/day (seven-day dermal dose) and 0.3 mg/kg/day (14-day dermal dose) were selected for short- and intermediate-term occupational risk assessment, respectively, while a dose level of 17.0 mg/kg/day (acute inhalation dose) was selected for assessment of occupational inhalation risk during any exposure duration.

An uncertainty factor (UF) of 100 was applied to all doses selected for risk assessment purposes to account for interspecies extrapolation (10x) and intraspecies variability (10x). An additional UF of 3x was applied to doses selected for acute dietary and inhalation risks because a NOAEL was not identified in the studies. The 10x FQPA safety factor was removed for all populations.

Acute and chronic dietary exposure from food was estimated for the general US population and various population subgroups with particular regard to infants and children. Aggregate acute and chronic risk assessments addressed the potential dietary exposure to oxydemeton-methyl residues from food and drinking water. The aggregate assessment for the general population and specific subgroups includes only food and water exposures because none of the registered uses are likely to involve applications to public access areas or residential sites other than soil injection by certified applicators to shade trees and ornamentals. HED also considered dermal and inhalation exposure to occupational pesticide handlers, mixers, loaders, applicators and postapplication workers during harvesting activities.

Tolerances for residues of oxydemeton-methyl in plant and animal commodities and processed food/feed items are presently expressed in terms of the combined residues of oxydemeton-methyl and its cholinesterase-inhibiting metabolites. Oxydemeton-methyl metabolites exhibiting properties of ChE inhibition include oxydemeton-methyl sulfone. Thus, HED has recommended that the current tolerance expression be revised such that oxydemeton-methyl and oxydemeton-methyl sulfone (ODMS) are the residues to be regulated in plant commodities and that oxydemeton-methyl is the residue to be regulated in animal commodities.

The acute and chronic dietary risk assessments reflect highly refined exposure assessments utilizing monitoring data from both the USDA/PDP and FDA Surveillance Monitoring programs. Where possible, available monitoring data were translated to related crops. Where no monitoring data were available, anticipated residues were estimated using field trial data. Appropriate processing and cooking study data were also used when available. Percent of crop treated data were included in the generation of the residue distribution files (RDF) and in the creation of point estimates for blended commodities.

The Environmental Fate and Effects Division (EFED) provided a screening level assessment using simulation models to estimate the potential concentration of oxydemeton-methyl in ground and surface water. Estimated surface water environmental concentrations were 0.6 ppb (average) and 11.7 ppb (maximum). The available environmental fate data suggest that oxydemeton-methyl degrades rapidly. Neither oxydemeton-methyl or its sulfone metabolite is expected to contaminate ground water or to persist or accumulate in surface water.

Aggregate acute and chronic dietary risk estimates associated with the consumption of oxydemeton-methyl do not exceed HED's level of concern. Based on a highly refined Tier 3 acute probabilistic analysis, the most highly exposed population subgroup (females 13+/nursing) represents 7.1% of the acute PAD at the 99.9th percentile of exposure. Based on a highly refined Tier 3 chronic analysis, the most highly exposed population subgroup (non-nursing infants <1 year) represents 5.3% of the chronic PAD. In the absence of monitoring data, conservative estimates of exposure to oxydemeton-methyl residues in drinking water using modeled, screening-level inputs indicate that relative to exposure in food, residues in drinking water would not contribute significantly to either acute or chronic aggregate risk.

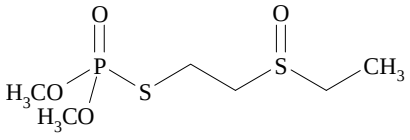
Occupational risk for handlers was assessed using data from the Pesticide Handler's Exposure Database (PHED). Risk associated with certain mixer/loader/applicator scenarios exceeds HED's level of concern for short-term and intermediate-term risk in a variety of exposure scenarios. For some scenarios involving application with a high-pressure handwand, low pressure handwand or backpack sprayer, further mitigation of risk using engineering controls is not feasible. No data were available to assess tree injection applications or mixing/loading/applying liquids using soil injection.

Postapplication risks were estimated using dislodgeable foliar residue (DFR) data for cauliflower, cotton, bell peppers, and sugar beets; however, standard values rather than activity-specific data were used to estimate residue transfer for crop/activity patterns. Restricted Entry Intervals (REI's), where the margins of exposure are NOT of concern for workers, are estimated to range from six to 59 days depending on the crop and postapplication activity. Current labels include an REI of 48 hours or 72 hours for regions where average rainfall is less than 25 inches/year.

The product/residue chemistry, exposure, and toxicology database for oxydemeton-methyl is adequate to assess risk (dietary risk to the general U.S. population and dermal/inhalation risk of occupational workers) from the agricultural use of oxydemeton-methyl with a reasonable level of confidence; these data also support reregistration. Additional product and residue chemistry data to meet guideline requirements are detailed in these disciplinary Chapters; these data remain outstanding.

2.0 PHYSICAL AND CHEMICAL PROPERTIES CHARACTERIZATION

Oxydemeton-methyl (S-[2-(ethylsulfinyl)-ethyl] O,O-dimethyl phosphorothioate) is an aliphatic, organophosphorous pesticide which is registered for use as a systemic acaricide and insecticide on a variety of food and non-food use sites. The molecular structure is:



Empirical Formula: $C_6H_{15}O_4PS_2$
Molecular Weight: 246.3 g/mole
CAS Registry No.: 301-12-2
Shaughnessy No.: 058702

Oxydemeton-methyl is a colorless to amber-colored liquid with a boiling point of 106°C. It is miscible with water; readily soluble (10-100 g/100 mL) in dichloromethane, 2-propanol, and toluene; and practically insoluble (<1 g/100 mL) in n-hexane. The vapor pressure is 5.1×10^{-5} mbar at 25°C. Because oxydemeton-methyl pure active ingredient (PAI) and technical grade of the active ingredient (TGAI) are not stable, oxydemeton-methyl is diluted with solvent to form a 50% ai formulation intermediate (FI) which is used to produce end-use product formulations. Preliminary analysis of the FI indicates that there are no impurities present or formed that would be of known toxicological concern.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Oxydemeton-methyl is an organophosphorous insecticide. In all of the toxicological studies evaluated, the no observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) was established by the inhibition of ChE. In acute toxicity studies with rats, oxydemeton-methyl exhibited high toxicity via the oral and dermal (Toxicity Category I; technical material) and inhalation (Toxicity Category II; end-use product) routes of administration. In rabbits, oxydemeton-methyl exhibited minimal primary eye and dermal irritation. For the chronic toxicity studies in the rat and dog, the developmental studies in the rat and rabbit, the reproductive toxicity studies in the rat, and the acute and subchronic neurotoxicity studies in the rat, inhibition of brain ChE activity was observed at the LOAEL in all of the studies.

In addition to ChE inhibition, the results of reproductive toxicity studies in the rat showed decreased male and female fertility of unknown origin. In these studies, absolute ovarian and testicular weights were decreased; males also had a high incidence of epididymal vacuolation at histopathological examination. These findings, coupled with positive results from some of the mutagenicity tests, resulted in several non-guideline studies designed to evaluate and elucidate potential adverse effects of oxydemeton-methyl on reproduction, particularly in the male. These special studies included evaluation of the reversibility of epididymal vacuolation in rats, a reproductive toxicity study with treated males and untreated females, and the determination of sperm counts, morphology and motility.

Even though oxydemeton-methyl was found to produce reproductive toxicity, it was not a developmental toxicant. There is no indication of increased sensitivity of the offspring of rats or rabbits after pre-natal and/or post-natal exposure to oxydemeton-methyl. In developmental toxicity studies, in both the rat and rabbit, oxydemeton-methyl did not produce any developmental toxicity at doses which produced maternal toxicity. Oxydemeton-methyl has been classified in “Group E” (i.e., the chemical is characterized as “Not Likely” to be carcinogenic in humans via relevant routes of exposure) because no compound-induced carcinogenic response was observed in mice or rats. In a rat metabolism study, urinary excretion was found to be the major route of elimination. In all, two major and five minor urinary metabolites were identified. Two of the minor metabolites, desmethyl ODM and desmethyl ODM sulfone, were believed to be biologically active and, in the absence of data to the contrary, were considered to be of toxicological concern. To resolve this question, the desmethylated metabolites were evaluated for their ability to inhibit brain ChE *in vitro*. In this study, brain ChE was not inhibited by either desmethyl ODM or desmethyl ODM sulfone over a wide concentration range; both oxydemeton-methyl and chlorpyrifos oxon (positive control) produced inhibition at very low concentrations.

3.2 Acute Toxicity

Acute toxicity values and categories for oxydemeton-methyl, technical and the manufacturing product Metasystox-R™ [50% ai in a stabilizer], are summarized in **Table 1**. As shown, oxydemeton-methyl technical is highly toxic (Toxicity Category I) via the oral and dermal routes of exposure. In a primary eye irritation study in rabbits, the technical was found to be slightly irritating (Toxicity Category III); however, the manufacturing product was found to be highly irritating (Toxicity Category I). The difference in this acute effect is likely due to the presence of a stabilizer.

Table 1. Acute Toxicity of ODM, Technical and Manufacturing Product, Metasystox-R™

Study Type	Animal	Results	Tox Cat	MRID No
ODM, Technical				
81-1: Acute Oral	Rat	Female: LD_{50} = 48 mg/kg	I	40779801
81-2: Acute Dermal	Rat	Female: LD_{50} = 112 mg/kg	I	00143350
81-4: Primary Eye Irritation	Rabbit	Slightly irritating	III	00151801
81-5: Primary Dermal Irritation	Rabbit	Non-irritating	IV	00151801
81-6: Dermal Sensitization	Guinea Pig	Not a skin sensitizer (Beuhler)	N/A	40779802
Metasystox-R (50% a.i. in a stabilizer)				
81-1: Acute Oral	Rat	Female: LD_{50} = 96 mg/kg	II	40779803C 40779803
81-2: Acute dermal	Rabbit	Male: LD_{50} = 844 mg/kg	II	40779804C 40779804
81-3: Acute Inhalation	Rat	Female: LC_{50} = 0.427 mg/L	II	40779805C 40779805
81-4: Primary Eye Irritation	Rabbit	Irritant (Probably caused by inerts)	I	40779806C 40779806
81-5: Primary Dermal Irritation	Rabbit	Very slightly irritating	IV	40779807C 40779807
81-6: Dermal Sensitization	Guinea Pig	Not a skin sensitizer (Beuhler)	N/A	40779802

3.3 FQPA Considerations

The HED FQPA Safety Factor Recommendation [Combined Report of the Hazard Identification Assessment Review Committee (HIARC) and Safety Factor Committee (SFC) and its Recommendation for the Organophosphates; August 6, 1998] that the 10x FQPA safety factor be retained because of a concern for heritable effects has been revised.

The Committee's earlier recommendation to retain the 10x safety factor was based on: (1) a concern for heritable effects as demonstrated in an *in vivo* mouse spot test which was positive for the induction of somatic cell mutations following intrauterine exposure of embryos; and (2) evidence of DNA strand breaks in rat testes cells in an *in vitro* alkaline elution assay (not confirmed *in vivo*). A mouse specific locus test was required.

[In its 60-day response to the preliminary risk assessment for oxydemeton-methyl, Gowan Company disagreed with EPA's rationale for imposition of the FQPA 10x safety factor and provided extensive technical comments in conjunction with a rebuttal submission to support their arguments specific to the mutagenicity testing in a rat alkaline in vivo germ cell assay. The Agency addressed the registrant's objections to retaining the 10x FQPA safety factor and informed Gowan that it was unable to reconsider the weight-of-evidence evaluation for potential heritable effects until such time definitive data were available that demonstrate that gonadal tissue was exposed to an adequate dose of oxydemeton-methyl in this study or in another appropriate germinal cell assay. Gowan provided a non-guideline, toxicokinetic study which was reviewed and found acceptable. The study data provided evidence that the existing in vivo alkaline elution assay of rat testes, which was negative for DNA strand breaks, should be reclassified as acceptable. The evidence provided in this study was considered by the HIARC on July 8, 1999, and the FQPA SFC on July 12, 1999.]

The FQPA Safety Factor Committee met on July 12, 1999, to re-evaluate the hazard and exposure data for oxydemeton-methyl in light of the recently submitted toxicokinetic data. Based on these new data (refer to Section 3.4 below for a full discussion), the Committee recommended that the FQPA safety factor be removed in assessing the risk posed by this chemical.

In considering the new data, the FQPA SFC concluded that a safety factor is not required for the following reasons:

- Based on the recently submitted toxicokinetic data and a weight-of-evidence re-evaluation of the genetic concerns resulting from exposure to ODM, the HIARC revoked the requirement for the mouse specific locus test which was previously identified as a data gap.

- The toxicity data base for ODM is now complete.

- The HIARC concluded that the genetic concerns resulting from exposure to ODM have been addressed.

Additional reasons for not retaining a safety factor for infants and children which were considered in previous SFC conclusions are as follows:

- There was no evidence of developmental effects being produced in fetuses at lower doses as compared to maternal animals nor was there evidence of an increase in severity of effects at or below maternally toxic doses following *in utero* exposure in the prenatal developmental toxicity studies in rats and rabbits;

- In the pre/postnatal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in pups when compared to parental animals (i.e., effects noted in offspring occurred at maternally toxic doses or higher);

- There was no evidence of abnormalities in the development of the fetal nervous system in the pre/postnatal studies submitted to the Agency; and

- Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary (food) exposure and to provide a screening level drinking water exposure assessment.

3.4 Endpoint Selection

On February 16, 1999, HED's Hazard Identification Assessment Review Committee (HIARC) reviewed the toxicology database for oxydemeton-methyl and selected doses and toxicology endpoints for risk assessment, based solely on **animal toxicity studies**. The HIARC evaluated the oxydemeton-methyl cholinesterase inhibition study in human volunteers (Doull et al, 1972; MRID 00039839) and concluded that the study alone is insufficient for endpoint selection or risk assessment. The dose regimen among the individual volunteers was of insufficient duration to demonstrate steady-state cholinesterase inhibition. Following evaluation of the comparative toxicology data in laboratory animals and humans, the HIARC concluded that the NOAEL identified in the one-year dog study based on plasma, RBC, and brain ChE inhibition be used, and the uncertainty factors for both interspecies variation and intraspecies extrapolation be applied.

The HIARC reconvened on July 8, 1999 to review recently submitted toxicokinetic data for oxydemeton-methyl. The toxicokinetic data showed that the exposure time (4 hours) in the *in vivo* rat alkaline elution assay was sufficient for oxydemeton-methyl to interact with the testes and, based on the findings of this study, the alkaline elution assay was upgraded to acceptable. The acceptability of the alkaline elution assay, in conjunction with the negative results of this assay as well as two dominant lethal studies, lowered the concern for heritable effects from exposure to oxydemeton-methyl and obliged the HIARC to evaluate the results of the mouse spot test more critically. The primary function of the mouse spot test is as a carcinogenesis screening tool. Although oxydemeton-methyl was positive in this test system, it was negative in other assays with somatic cells. In addition, oxydemeton-methyl has been shown to be non-carcinogenic in CD-1 mice and Fischer 344 rats. Based on a weight-of-evidence re-evaluation, the HIARC concluded that the genetic concerns resulting from exposure to ODM have been addressed and that the requirement for the mouse specific locus test be revoked. Therefore, the toxicity data base for ODM is now complete.

The doses and toxicological endpoints selected for various exposure scenarios are summarized in **Table 2**. For each of the exposure scenarios, toxicology endpoints have been selected for risk assessment purposes. The selected toxicology endpoints are consistent with organophosphate-induced toxicity (i.e., inhibition of ChE and resulting clinical signs of intoxication) and the studies selected are appropriate for the route and duration of exposure. The acute reference dose (RfD) is based on an acute neurotoxicity study in which rats received a single oral gavaged dose of oxydemeton-methyl; the effects observed were, therefore, attributable to a single oral dose. The chronic RfD is based on a chronic one-year study in which dogs received daily oral doses of oxydemeton-methyl. Special ChE dermal toxicity (route-specific) studies of seven- and 14-day durations, specifically address the short- and intermediate-term dermal exposure scenarios. The 14-day NOAEL used for intermediate-term dermal exposure risk assessment is considered representative of exposure durations up to several months because brain ChE inhibition effects were also seen in longer term oral dosing durations (90-days). The LOAELs resulting from longer term dosing durations, when adjusted for a 50% dermal absorption factor and an additional 3x uncertainty factor for lack of a NOAEL, are equivalent to the NOAEL established in the 14-day dermal study.

Table 2. Summary of Doses and Toxicological Endpoints for Oxydemeton-methyl Risk Assessment

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	LOAEL=2.5	Decreased RBC and brain ChE activity in males at day 0.	Acute Neurotoxicity in the rat
	UF=300 (10 X 10 X 3)	**Acute RfD = 0.008 mg/kg/day**	
	FQPA Safety Factor Reduced (1x)	**Acute PAD = 0.008 mg/kg/day**	
Chronic Dietary	NOAEL=0.0125	Decreased erythrocyte and brain ChE	Chronic dog
	UF=100 (10 X 10)	**Chronic RfD = 0.000125 mg/kg/day**	
	FQPA Safety Factor Reduced (1x)	**Chronic PAD = 0.000125 mg/kg/day**	
Carcinogenicity (Dietary)	OMD is classified as a **"Not Likely"** human carcinogen.		
Short-Term (Dermal)	NOAEL=5.0	Decrease plasma, RBC and brain ChE	7-Day dermal toxicity study in the rat
	UF = 100 (10 X 10) for occupational populations; no residential uses exist.		
Intermediate-Term (Dermal)	NOAEL= 0.3	Decreased brain ChE	14-Day dermal toxicity study in the rat
	UF = 100 (10 X 10) for occupational populations; no residential uses exist.		
Inhalation (any time period)	LOAEL = 0.177 mg/L (17.02 mg/kg/day)	Clinical signs (tremors)	Acute Inhalation Study in the Rat
	UF = 300 (10 X 10 X 3) for occupational populations; no residential uses exist.		

4.0 EXPOSURE AND RISK CHARACTERIZATION

4.1 Summary of Registered Uses

Oxydemeton-methyl is a restricted use pesticide. At this time, products containing oxydemeton-methyl are intended solely for occupational use. None of the registered occupational uses are likely to involve applications to public access areas or at residential sites other than soil injection by certified applicators to shade trees and ornamentals. Oxydemeton-methyl is used to control aphids, mites, leafhoppers, thrips, corn rootworm beetles and lygus bugs on beans (lima), broccoli, broccoli raab, Brussels sprouts, cabbage, cauliflower, corn (sweet), cotton, cucumbers, eggplant, grapefruit, lemons, lettuce (head), melons (including muskmelons), oranges, peppermint, peppers, pumpkins, spearmint, squash (summer and winter), strawberries, sugar beets, walnuts, and watermelons. Oxydemeton-methyl is also registered for bark treatment on filberts, for treatment of nonbearing apples, apricots, cherries, crabapples, grapes, nectarines, peaches, plums/prunes, and quinces, for treatment of alfalfa and clover seed crops, application to Christmas tree plantations, ornamental flowering plants, woody shrubs, and various ornamental and shade trees.

Oxydemeton-methyl is formulated as a 2 lb/gal emulsifiable concentrate (EC) formulation (25% ai) and as a liquid ready-to-use formulation (50% ai) for tree injections. Depending on the crop or site, up to three applications per season may be made using airblast sprayers, ground boom sprayers, or by bark treatment (e.g., brush-on or tree injection), soil injection and chemigation. Closed systems for mixing and loading must be used for all aerial application and chemigation systems.

4.2 Dietary Exposure

Potential exposure to oxydemeton-methyl residues in the diet occurs through food and water sources. Depending on the crop, one to three foliar applications of oxydemeton-methyl may be made per season. The field trial residue data supporting reassessed tolerances indicate there are quantifiable residues on edible crops; approximately half the tolerance levels are set based on true detects in the residue data set and there is a likelihood of residue transfer to meat and milk. Based on laboratory studies, oxydemeton-methyl is not likely to persist in surface water or expected to leach to ground water. Screening-level model estimates indicate the contribution of oxydemeton-methyl residues to dietary exposure through drinking water does not result in an aggregate (food + water) exposure concern.

Revisions to the acute and chronic dietary (food) exposure assessment for oxydemeton-methyl through food include an evaluation using Dietary Exposure Evaluation Model (DEEM$^{TM)}$ software and consumption data from the 1989-1992 Continuing Survey of Food Intakes (CSFII). The revised analysis also incorporates new percent of crop treated data, anticipated residue refinements using USDA Pesticide Data Program (PDP) and Food and Drug Administration (FDA) monitoring data, residue field trial and cooking study data, and processing factors where available. Also considered in HED's revision was a second acute probabilistic analysis submitted by the registrant. In its second submission, Gowan Company addressed some but not all of the deficiencies identified in HED's review (D249562; MRID 44594401) of a previously submitted acute probabilistic analysis for ODM. Although Gowan's second submission (D253178; MRID 44748501) was also found to be insufficient for regulatory purposes, HED incorporated portions of the registrant's residue data files into its revised acute dietary analysis.

The previous dietary risk analyses conducted by HED, included the 10x factor for protection of infants and children as required by FQPA. Based on new toxicity data, HED's FQPA Safety Factor Committee recommended that the 10x safety factor be removed. Thus, the FQPA 10x safety factor was not applied to the revised acute and chronic dietary risk assessment. The chronic dietary risk was additionally revised using doses and toxicological endpoints based solely on animal toxicity studies.

Tolerances for residues of oxydemeton-methyl in/on plant and animal commodities and processed food/feed items are presently expressed in terms of the combined residues of oxydemeton-methyl and its cholinesterase inhibiting metabolites. Based on the available plant and animal metabolism studies, the HED Metabolism Committee determined that oxydemeton-methyl and oxydemeton-methyl sulfone (ODMS) are the residues to be regulated in plant commodities and that oxydemeton-methyl is the residue to be regulated in animal commodities. Adequate analytical methods are available for the purposes of tolerance enforcement (Pesticide Analytical Manual [PAM] Vol. II).

Residue data from crop field trials, processing studies, and livestock feeding studies have been reviewed for the purpose of tolerance reassessment. HED has high confidence in the available geographically representative field trial data. HED is recommending revocation of tolerances for certain commodities for one or more of the following reasons: (1) there are no longer significant livestock feed items for the commodity; (2) use on non-bearing fruit trees is a non-food use based on the current use pattern; (3) currently there are no registered uses; and (4) tolerances for commodities from crops which have

been removed from Gowan's marketing label may be revoked pending the Agency's decision to reinstate these uses.

4.2.1 Dietary Exposure (food source)

The acute and chronic dietary (food) exposure assessment was conducted using the DEEM^{TM}, which incorporates consumption data generated in USDA's Continuing Survey of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three-day average of consumption for each sub-population is combined with residues in commodities to determine average exposure in mg/kg/day. For acute dietary risk assessments, the entire distribution of single day food consumption events is combined with either a single residue level (deterministic analysis) or a distribution of residues (probabilistic analysis, referred to as "Monte Carlo") to obtain a distribution of exposure in mg/kg/day. For deterministic (Tier 1) acute analyses, the Agency uses the 95th percentile of exposure as a threshold for concern; when probabilistic assessments are conducted, the Agency uses the 99.9th percentile of exposure as a threshold for concern. Tier 3 analyses were performed for the acute and chronic dietary exposure evaluation of oxydemeton-methyl. Both assessments are considered to be highly refined.

From the tolerance listing, apples, grapes, plums (prunes), and apricots have been excluded from the risk assessment since the use pattern for these commodities is considered to be a "nonfood" use (tolerances for these crops will be revoked as part of tolerance reassessment). Registrations for blackberries, raspberries, potatoes, and peas are not being supported for reregistration and also have been excluded from the risk assessment (tolerances will be revoked). Citrus, field corn, popcorn, sorghum, safflower, onions, pears, turnips, and snap beans have been deleted from the current marketing labels (but NOT removed from the Manufacturing Use Product label). At the request of SRRD, these deleted commodities have been retained in this risk assessment. In addition to the above commodities, ODM risk assessment is based on broccoli, brussels sprouts, cabbage, cauliflower, cotton, cucurbits, filberts, melons, mint, pears, peppers, safflower, strawberries, sugar beets, sweet corn, walnuts, milk, and meat products. For chronic risk estimates, HED used mean residue values from field trials for cottonseed, eggplant, filbert, peppers, safflower, mint, strawberry, and sugar beets.

4.2.2 Chronic Dietary Exposure Assessment

The Tier 3 DEEM™ chronic dietary exposure assessment for oxydemeton-methyl included use of weighted average percent crop treated data (BEAD QUA, I. Yusuf, 11/10/98) and anticipated residues developed using residue data from available crop field trials and livestock feeding studies, and PDP/USDA FDA monitoring data (S. Piper and C. Christensen, 6/20/99). Where percent crop treated estimates indicated little or no oxydemeton-methyl use (including but not limited to crops deleted from Gowan's marketing label in 1994), HED applied a default minimum assumption of 1% crop treated. Although actual usage data indicating <1% crop treated are available from BEAD for use in dietary risk analysis, it is not currently HED's policy to use such data in its DEEM™ models for Tier 2 or 3 assessments.

Chronic exposure estimates were compared to the oxydemeton-methyl chronic Population Adjusted Dose (cPAD) of 0.000125 mg/kg/day. This cPAD is based on a NOAEL of 0.0125 mg/kg/day from a chronic dog study which demonstrated RBC and brain ChE depression following oral dosing and uncertainty factors of 10x for intraspecies variability and 10x for interspecies extrapolation. The FQPA safety factor was removed (1x), thus the RfD and the cPAD are numerically equivalent. The results of these analyses are presented in **Table 3**.

Table 3. Summary Chronic Dietary Exposure and Risk Estimates for Oxydemeton-methyl

Population Subgroup	Anticipated Residue Concentration (mg/kg/day)	Percent of Chronic PAD[a]
U.S. Population	0.000003	2.0
All Infants (<1 year)	0.000005	4.0
Nursing Infants (<1 year)	0.000001	1.0
Non-nursing Infants (<1 year)	0.000007	5.3
Children (1-6 years)	0.000006	4.5
Children (7-12 years)	0.000004	3.3

[a]The cPAD is 0.00013 mg/kg/day for all population subgroups.

Chronic dietary exposure to oxydemeton-methyl results in risk estimates that are considerably below the Agency's level of concern. Chronic exposure estimates were highest for non-nursing infants (<1 year) and consumed 5.3% of the cPAD for this population subgroup. General U.S. population exposure estimates consumed 2.0% of the cPAD.

4.2.3 Acute Dietary Exposure Assessment

The Tier 3 DEEM™ acute probabilistic dietary exposure assessment for oxydemeton-methyl included use of maximum average percent crop treated data (BEAD QUA, I. Yusuf, 11/10/98) and anticipated residues developed using residue data from available crop field trials and livestock feeding studies, and USDA/PDP and FDA monitoring data (S. Piper and C. Christensen, 6/20/99).

Acute exposure estimates were compared to the oxydemeton-methyl acute Population Adjusted Dose (aPAD) of 0.008 mg/kg/day. This aPAD is based on a LOAEL of 2.5 mg/kg/day from an acute neurotoxicity study in the rat which demonstrated RBC and brain ChE depression following a single oral dose and uncertainty factors of 10x for intraspecies variability, 10x for interspecies extrapolation, and 3x for lack of a NOAEL. The FQPA safety factor was removed (1x); thus, the acute RfD and the acute PAD are numerically equivalent. The results of these analyses are presented in **Table 4**.

Table 4. Summary of Acute Dietary Exposure and Risk Estimates for Oxydemeton-methyl[a]

Population Subgroup	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure (mg/kg/d)	%aPAD	Exposure (mg/kg/d)	%aPAD	Exposure (mg/kg/d)	%aPAD
General US Population	0.000020	0.24	0.000053	0.66	0.000279	3.49
Females 13+/nursing	0.000019	0.24	0.000052	0.65	0.000568	7.10
Males 13-19	0.000018	0.22	0.000049	0.62	0.000143	1.79
Males 20+	0.000011	0.14	0.000025	0.31	0.000210	2.62
All Infants <1yr	0.000025	0.31	0.000054	0.67	0.000279	3.49
Nursing Infants <1 yr	0.000006	0.08	0.000034	0.42	0.000245	3.07
Non-Nursing Infants <1 yr	0.000027	0.33	0.000056	0.70	0.000168	2.09
Children (1-6 years)	0.000051	0.6	0.000123	1.54	0.000510	6.37
Children (7-12 years)	0.000036	0.45	0.000082	1.03	0.000388	4.85

[a]The aPAD is mg/kg/day for all population subgroups.

Acute dietary exposure to oydemeton-methyl results in risk estimates that are considerably below the Agency's level of concern. Acute exposure estimates were highest for females 13+/nursing and consumed 7.1% of the aPAD at the 99.9th percentile of exposure. The general U.S. population exposure estimates consumed 3.5% of the aPAD.

4.3 Dietary Exposure (drinking water source)

At the present time, sufficient monitoring data are not available to perform a quantitative drinking water assessment for oxydemeton-methyl. However, EFED provided two screening level drinking water assessments (EFED memos by Costello and Wells, 9/11/97 and Breithaupt and Lin, 6/14/99). These assessments utilized PRZM-EXAMS and SCI-GROW (Screening Concentrations in Ground Water) screening models to provide estimates of surface and ground water concentrations of oxydemeton-methyl. Based on laboratory studies, neither oxydemeton-methyl or its metabolite of toxicological concern, ODMS, is expected to persist in surface water or expected to leach to ground water. Thus, oxydemeton-methyl was used as a surrogate for ODMS in EFED's screening analyses.

Surface Water. The PRZM-EXAMS models predict a maximum oxydemeton-methyl surface water peak concentration of 11.7 ppb and a maximum long-term mean concentration of 0.6 ppb. These values represent upper-bound estimates of the concentrations that might be found in surface water due to use of oxydemeton-methyl based on simulations performed using the maximum application rates of 1.50-3.76 lb/ai/A applied three times/year with seven to 14 day intervals between applications. The model input for aerobic soil metabolism half-life was 9.6 days.

Ground Water. The SCI-GROW model predicts an estimated maximum concentration in ground water of 0.008 μg/L. The SCI-GROW model is a screening model used to estimate concentrations of pesticide in ground water under "worst case" conditions. The SCI-GROW model is based on scaled groundwater concentration from ground water monitoring studies, environmental fate properties (aerobic soil metabolism half-lives and sorption coefficients) and application rates. The current version of SCI-GROW appears to provide realistic estimates of pesticide concentrations in shallow, highly vulnerable groundwater (i.e., sites with sandy soils and depth to groundwater of 10 to 20 feet).

Limited monitoring data indicate that oxydemeton-methyl has not been detected in ground and surface water samples at detection limits of 0.1 and 0.5 ppb. The estimated environmental concentrations (EECs) for ground and surface water are greater than these detection limits, thus indicating that the models are not likely to underestimate the potential for oxydemeton-methyl residues in drinking water.

4.3.1 Chronic and Acute DWLOCs

Drinking Water Levels of Comparison (DWLOCs) represent the maximum contribution to the human diet, in mg/kg/day, that may be attributed to residues of a pesticide in drinking water after dietary exposure. OPP uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. DWLOC values are not regulatory standards for drinking water. They do have indirect regulatory implications through aggregate exposure and risk assessments.

Chronic and acute drinking water levels of comparison (DWLOC) were calculated based on dietary (food) exposure (chronic and acute) and standard body weights and water consumption figures. The Agency's standard body weights and water consumption values used to calculate DWLOCs are as follows: 70kg and 2L/day (adult male), 60 kg and 2L/day (adult female), and 10 kg and 1L/day (child). To calculate chronic and acute DWLOCs, the chronic and acute dietary food exposure was subtracted from the cPAD and aPAD, respectively, using the equation:

$$DWLOC_{chronic\ or\ acute} = \frac{[\text{chronic or acute water exposure (mg/kg/day)} \times \text{(body weight)}]}{[\text{consumption (L)} \times 10^{-3}\ \text{mg}/\mu\text{g}]}$$

where, chronic water exposure (mg/kg/day) = [cPAD - chronic food (mg/kg/day)];

or, where acute water exposure (mg/kg/day) = [aPAD - acute food (mg/kg/day)].

The results are summarized in **Tables 5 and 6**. Comparisons are made between DWLOCs and the screening-level estimated concentrations of oxydemeton-methyl in surface water and ground water using PRZM/EXAMS and SCI-GROW models, respectively.

Table 5. Summary of Chronic DWLOC Calculations

Population Subgroup	PRZM-EXAMS (μg/L)	SCI-GROW (μg/L)	cPAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Chronic H_2O Exposure (mg/kg/day)	$DWLOC_{chronic}$ (μg/L)
Adult Male	0.6	0.008	0.000125	0.000003	0.000122	4
Adult Female	0.6	0.008	0.000125	0.000002	0.000123	4
Infants <1 yr	0.6	0.008	0.000125	0.000005	0.000120	1
Children 1-6	0.6	0.008	0.000125	0.000006	0.000119	2

Chronic DWLOCs. As shown in **Table 5**, the drinking water estimated concentrations in ground water (0.008 ppb) and surface water (0.6 ppb) are below HED's chronic DWLOCs for oxydemeton-methyl. HED concludes that based on the available information, modeled residues in drinking water indicate that the contribution to chronic dietary exposure does not result in an aggregate risk concern.

Table 6. Summary of Acute DWLOC Calculations

Population Subgroup	PRZM-EXAMS (μg/L)	SCI-GROW (μg/L)	aPAD (mg/kg/day)	Acute Food Exposure (mg/kg/day)	Acute H_2O Exposure (mg/kg/day)	$DWLOC_{acute}$ (μg/L)
Adult Male	11.7	0.008	0.008	0.000210	0.00779	273
Adult Female	11.7	0.008	0.008	0.000568	0.007432	223
Infants <1 yr	11.7	0.008	0.008	0.000279	0.007721	77
Children 1-6	11.7	0.008	0.008	0.000510	0.00749	75

Acute DWLOCs. As shown in **Table 6**, the drinking water estimated concentrations in ground water (0.008 ppb) and surface water (11.7 ppb) are considerably below HED's DWLOCs for oxydemeton-methyl. HED concludes that based on the available information, modeled residues in drinking water indicate that the contribution to acute dietary exposure does not result in an aggregate risk concern.

4.4 Non-Dietary Exposure

Gowan Company submissions (MRID's 44783101 and 44806801) received during the public comment period have been considered in this revised non-dietary exposure assessment. The current assessment has been revised to reflect further refinement of the handler and postapplication exposure assessments, which are in part based on the recent information provided by Gowan Company. The revisions include: (1) the expansion of crop groups for handler scenarios to reflect the maximum application rate of 0.5 lb ai/A for cole crops; and (2) further assessment of postapplication exposures, which relies on the applicability of study data extrapolated to crops for which no dislodgeable residue data are currently available. In addition, the postapplication risk assessment was modified to include standard transfer coefficients for postapplication agricultural activities (HED Science Advisory Council for Exposure; Draft Policy.003).

There are potential occupational exposures to handlers (those mixing and loading) and to workers when applying oxydemeton-methyl or during postapplication activities such as harvesting and scouting. Occupational handlers and workers are potentially exposed via dermal and inhalation routes; however, inhalation exposure during postapplication activities is considered to be minimal for oxydemeton-methyl. The exposure duration may be short-term (one to seven days) and intermediate-term (one week to several months). A long term exposure duration is not expected for either applicators or postapplication workers because the maximum number of applications is limited to three per season for most use sites and to one or two per season for the remaining use sites.

Oxydemeton-methyl is a restricted use pesticide that is only applied by certified applicators. There are no registered uses of oxydemeton-methyl in residential settings and none of the registered occupational uses are likely to involve applications to public access areas or at residential sites other than soil injection by certified applicators to shade trees and ornamentals. There may be potential for spray drift associated with aerial applications or other high volume spray in densely populated agricultural areas where peripheral residential exposure and/or exposure to farmworker children could occur. An assessment of the potential exposure and risk from spray drift associated with the agricultural use of oxydemeton-methyl has not been included in this document. The Agency is in the process of developing guidance and procedures for characterizing these kinds of exposures. This guidance will be included in upcoming revised SOPs for Residential Exposure Assessment anticipated in 1999.

4.4.1 Occupational Handler Exposure Scenarios

HED has identified 13 major exposure scenarios for which there is potential for occupational handler exposure during mixing, loading, and applying products containing oxydemeton-methyl to agricultural crops and to non-agricultural use sites. These occupational scenarios reflect a broad range of application equipment and use sites, and were classified as either short-term or intermediate term based primarily on the frequency of exposure. The estimated exposures considered baseline protection (long pants and a long-sleeved shirt, no gloves, and an open cab or tractor), additional personal protective equipment (PPE, which includes a double layer of clothing and gloves), and engineering controls (closed application, closed mixing systems, and water soluble bags). NOTE: *Exposure/risk estimates have been conducted for water soluble bags* (gel packs) *for mitigation purposes only; this type of formulation packaging is* not *listed on the most current labels and based on recent information from the registrant, development of such packaging may not be feasible.*

4.4.1.1 Occupational Handler Exposure Data Sources and Assumptions

The chemical specific handler studies (MRID's 00158006 and 41201701) submitted to the Agency were found to be unacceptable for reregistration purposes and were not used to estimate exposures. In cases where chemical specific monitoring data are unavailable or unacceptable, HED uses the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures; therefore, the exposure analysis for oxydemeton-methyl was conducted using data from PHED.

PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., wettable powders, granulars), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing). While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handler) may not accurately represent labeled used in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments.

In addition to the use of standard unit exposure values based on the PHED database, the following assumptions and factors were used to complete the exposure assessment for oxydemeton-methyl:

- Maximum label rates for representative crops.
- Average body weight of an adult handler is 70 kg.
- Average work day interval represents an 8-hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).
- Daily acres and volumes (as appropriate) to be treated in each scenario include:
  - 350 acres for aerial and chemigation applications (including flaggers supporting aerial applications);
  - 80 acres for groundboom applications;
  - 20 acres for high-pressure handwand;
  - 5-10 gallons per day for brush-on bark applications;
  - 40 gallons per day for low-pressure handwand;
  - 40 acres for airblast applications to grapes; and
  - 20 acres for airblast applications to tree crops (20 rather than 40 acres was used because the volume/acre is relatively high).

4.4.1.2 Occupational Handler Risk Characterization

Margins of Exposure (MOE) were derived based upon comparison of dermal exposure estimates against NOAEL's of 5 mg/kg/day for short-term exposure or 0.3 mg/kg/day for intermediate-term exposure. Both short and intermediate-term NOAEL's were from dermal toxicity studies in the rat. MOE's were also derived based upon comparison of inhalation exposure estimates against a LOAEL of 0.177 mg/L (0.0989 mg ai/L or 17.02 mg/kg/day). A common toxicological endpoint exists (i.e., neurotoxicity) for the dermal and inhalation routes. However, because the uncertainty factors are dissimilar (i.e., 100 for the dermal route, and 300 for the inhalation route), the MOE's were combined using the aggregate risk index (ARI) method. ARI's, which are ratios (of the MOE to the uncertainty factor) adjusted to a common denominator of one, are calculated using the following formula:

ARI = 1 / {[1 / (Dermal MOE/Dermal UF)] + [1 / (Inhalation MOE/Inhalation UF)]}

An ARI is compared to an uncertainty factor of 1; an ARI of less than one is indicative of a risk concern for adverse health effects.

It should be noted that estimated inhalation risk for all exposure time frames is a relatively minor component of the combined dermal and inhalation risk estimates expressed as ARI's. For example, inhalation MOE's generally ranged about 1,000 to 40,000. When an inhalation MOE of 1,000 is combined with a dermal MOE of 4.7, the ARI is 0.047. Except for mixing/loading/applying liquids as a tree bark treatment using a paintbrush, inhalation MOE's alone were typically well above HED's level of inhalation risk concern. For this single scenario of inhalation risk concern, the inhalation MOE alone was 210; the ARI was 0.00097.

Short-Term Risk Characterization. When short-term dermal and inhalation risks (MOE's) are combined and uncertainty factors are normalized as an ARI, all but two of the 13 major exposure scenarios reflecting baseline protective clothing result in exposure/risk margins which exceed HED's level of concern. For the two scenarios not of risk concern [(5) application of sprays with a groundboom and (13) flagging aerial sprays], ARI's ranged from 1.1 to 5.5. For those remaining scenarios of risk concern, ARI's ranged from one to three orders of magnitude <1.

Short-term exposure and risk is mitigated by additional PPE for many of the remaining scenarios and the use of engineering controls, where feasible, further mitigates short-term exposure and risk resulting in ARI's >1 for many but not all scenarios. **Four scenarios remain where risk estimates, expressed as ARI's, exceed HED's level of concern:**

(7) applying liquids using a high pressure handwand (ARI = 0.4);
(8) mixing/loading/applying liquids as a tree bark treatment using a paint brush (ARI = 0.008);
(11) backpack sprayer/knapsack (ARI = 0.07); and
(12) low pressure handwand (ARI = 0.3).

Intermediate-Term Risk Characterization. When intermediate-term dermal and inhalation risks (MOE's) are combined and uncertainty factors are normalized as an ARI, all of the 13 major exposure scenarios reflecting baseline protective clothing and the use of additional PPE result in exposure/risk margins which exceed HED's level of concern. Using engineering controls where feasible, intermediate-term ARI's are >1 for only three scenarios. Intermediate-term risk estimates, expressed as ARI's, for all other scenarios exceed HED's level of concern.

A summary of the short-term and intermediate-term ARI's for baseline, additional PPE, and engineering controls is presented in **Table 7**.

Table 7. Short-term and Intermediate-term Aggregate Risk Indices for ODM at Baseline and with Mitigation Measures

Exposure Scenario (Scenario #)	Baseline					Additional PPE					Engineering Controls				
	Inhalation MOE [a]	Short-term		Intermediate-term		Inhalation MOE [a]	Short-term		Intermediate -term		Inhalation MOE [e]	Short-term		Intermediate-term	
		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]
Mixer/Loader Exposure and Dose Levels															
Mixing/Loading Liquid Formulations for Aerial/Chemigation Application (1a)	2,800	0.34	0.0034	0.021	0.00021	2,800	59	0.55	3.5	0.035	41,000	120	1.2	7.0	0.07
	3,800	0.46	0.0046	0.028	0.00028	3,800	78	0.73	4.7	0.047	55,000	160	1.6	9.3	0.093
	5,700	0.69	0.0069	0.041	0.00041	5,700	120	1.1	7.1	0.071	82,000	230	2.3	14	0.14
	7,600	0.92	0.0092	0.055	0.00055	7,600	160	1.5	9.4	0.094	110,000	310	3.1	19	0.19
Mixing/Loading Liquid Formulations for Groundboom Application (1b)	12,000	1.5	0.015	0.091	0.00091	12,000	260	2.4	15	0.15	180,000	510	5.1	31	0.31
	17,000	2.0	0.02	0.12	0.0012	17,000	340	3.2	21	0.21	240,000	680	6.7	41	0.41
	25,000	3.0	0.03	0.18	0.0018	25,000	510	4.8	31	0.31	360,000	1,000	9.9	61	0.61
	33,000	4.0	0.04	0.24	0.0024	33,000	690	6.5	41	0.41	480,000	1,400	14	81	0.81
Mixing/Loading Liquid Formulations for Airblast Sprayer (1c)	44,000	5.4	0.054	0.32	0.0032	44,000	920	8.7	55	0.55	640,000	1,800	18	110	1.1
	66,000	8.0	0.080	0.48	0.0048	66,000	1,400	13	82	0.82	960,000	2,700	27	160	1.6
Mixing/Loading Liquid Formulations for High-Pressure Handwand (1d)	44,000	5.4	0.054	0.32	0.0032	44,000	920	8.7	55	0.55	640,000	1,800	18	110	1.1

Exposure Scenario (Scenario #)	Baseline					Additional PPE					Engineering Controls				
	Inhalation MOE [a]	Short-term		Intermediate-term		Inhalation MOE [a]	Short-term		Intermediate -term		Inhalation MOE [e]	Short-term		Intermediate-term	
		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]
Mixing/Loading Water-soluble Bags (Gel Packs) for Aerial/Chemigation Application (2a)	See Engineering Controls			See Engineering Controls		See Engineering Controls			See Engineering Controls		19,000	140	1.4	8.2	0.082
											28,000	200	2.0	12	0.12
											38,000	270	2.6	16	0.16
Mixing/Loading Water-soluble Bags (Gel Packs) for Groundboom Application (2b)											83,000	600	5.9	36	0.36
											120,000	890	8.7	54	0.54
											170,000	1,200	12	71	0.71
Mixing/Loading Water-soluble Bags (Gel Packs) for Airblast Sprayer (2c)											220,000	1,600	16	95	0.95
											330,000	2,400	23	140	1.4
Mixing/Loading Water-soluble Bags (Gel Packs) for High-Pressure Handwand (2d)											220,000	1,600	16	95	0.95
Applicator Exposure and Dose Levels															
Applying Sprays with Fixed-wing Aircraft (3)	See Engineering Controls			See Engineering Controls		See Engineering Controls			See Engineering Controls		67,000	270	2.7	16	0.16
											100,000	400	4.0	24	0.24
Applying Sprays with Helicopter Aircraft (4)	See Engineering Controls			See Engineering Controls		See Engineering Controls			See Engineering Controls		2,500,000	700	7.0	42	0.42
											3,800,000	1,100	11	63	0.63
Applying Sprays with a Groundboom (5)	27,000	420	4.0	25	0.25	27,000	530	5.0	32	0.32	460,000	1,200	12	70	0.70
	40,000	630	6.0	38	0.38	40,000	800	7.5	48	0.48	690,000	1,800	18	110	1.1
Applying Sprays Using an Airblast (6)	12,000	43	0.43	2.6	0.026	12,000	71	0.7	4.2	0.042	120,000	820	8.0	49	0.49
	18,000	65	0.64	3.9	0.039	18,000	110	1.1	6.4	0.064	180,000	1,200	12	74	0.74
Applying Using a High-Pressure Handwand (7)	670	8.6	0.083	0.52	0.0052	670	43	0.36	2.6	0.026	Not Feasible			Not Feasible	
Mixing/Loading/Applying Liquids as a Tree Bark Treatment Using a Paintbrush (8)	210	0.097	0.00097	0.0058	0.000058	210	0.80	0.0079	0.048	0.00048	Not Feasible			Not Feasible	
	430	0.19	0.0019	0.012	0.00012	430	1.6	0.016	0.095	0.00095	Not Feasible			Not Feasible	

Exposure Scenario (Scenario #)	Baseline					Additional PPE					Engineering Controls				
	Inhalation MOE [a]	Short-term		Intermediate-term		Inhalation MOE [a]	Short-term		Intermediate -term		Inhalation MOE [e]	Short-term		Intermediate-term	
		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]		Dermal MOE [b]	ARI [c]	Dermal MOE [d]	ARI [c]
Tree Injection (Ready-to-Use Liquid) (9)	No Data			No Data		No Data			No Data		No Data			No Data	
Mixer/Loader/Applicator Exposure and Dose Levels															
Soil Injection (10)	No Data			No Data		No Data			No Data		No Data			No Data	
Backpack Sprayer/Knapsack (11)	1,300	4.7	0.046	0.28	0.0028	1,300	73	0.072	0.44	0.0044	Not Feasible			Not Feasible	
Low Pressure Handwand - liquid(12)	1,300	0.12	0.0012	0.007	0.000070	1,300	32	0.3	1.9	0.019	Not Feasible			Not Feasible	
Flagger Exposure and Dose Levels															
Flagging Aerial (Sprays) (13)	13,000	120	1.2	7.3	0.073	13,000	130	1.3	8.0	0.08	650,000	6,100	59	360	3.6
	19,000	180	1.8	11	0.11	19,000	200	1.9	12	0.12	970,000	9,100	89	550	5.5

Note: An ARI greater than 1 is considered acceptable.

[a]Baseline inhalation MOE's were used to calculate both Baseline and Additional PPE ARI's because they were considered acceptable (i.e., greater than 300) without the addition of respirator protection factors.

[b]Short-term Dermal MOE's for Baseline, Additional PPE, and Engineering Controls. Baseline dermal unit exposure represents long pants, long sleeve shirt, no gloves, open mixing/loading, and open cab tractor.

Additional PPE:

1a, 1b, 1c, 1d, 5, 6, 7, 8, 11, and 12:	double layer clothing (Protection Factor = 50% for the second layer) with chemical resistant gloves
13:	double layer clothing (Protection Factor = 50% for the second layer)

Engineering Controls:

1a, 1b, 1c, and 1d:	closed mixing system, single layer of clothing and chemical resistant gloves
2a, 2b, 2c, and 2d:	water-soluble bags (gel packs), single layer clothing, chemical resistant gloves
3, 4:	enclosed cockpit, single layer clothing, and no gloves
5:	enclosed cab, single layer clothing, and no gloves
6:	enclosed cab, single layer clothing and chemical resistant gloves
13:	enclosed truck (Protection Factor = 98%), single layer clothing, no gloves

[c]ARI = 1/{[1/(Dermal MOE/Dermal UF)] + [1/(Inhalation MOE/Inhalation UF)]} where the target ARI is 1.
[d]Intermediate-term Dermal MOE's for Baseline, Additional PPE, and Engineering Controls. Clothing scenarios are the same as those for short-term dermal MOE.
[e]Inhalation MOE's for Engineering Controls.

Additional PPE:

8:	dust mist (D/M) respirator; the vapor pressure of ODM is 2.85 E-05 Torr at 20°C.
9:	

Engineering Controls:

1a, 1b, 1c, and 1d:	Closed mixing/loading system
2a, 2b, 2c, and 2d:	Water-soluble bags or gel packs
3, 4 :	Enclosed cockpit
5, 6:	Enclosed cab
13:	Enclosed truck

A number of issues must be considered when interpreting the occupational short- and intermediate-term risk estimates.

- PHED values are approximately median exposures (i.e., central tendency point estimates) over the available data. That is, 50 percent of workers doing the same activity would be expected to have *higher* unit exposures, and 50 percent would be expected to have *lower* unit exposures. These values are derived from actual exposure studies where the same formulation types, equipment, and methods were employed as are used for oxydemeton-methyl. Typically, there is high variability among replicates in exposure studies, often covering a range of orders of magnitude. EPA considers unit exposure values derived from PHED to be no higher than average or central tendency values.

- Recommended application rates vary by up to only a factor of two on the label (e.g., from 1.5 to 3 pints/acre), while for some crops only a single rate is listed. Thus, the dermal and inhalation exposure estimates should be considered close to typical, rather than conservative or "high-end" bounding-type estimates. Back-calculations indicate that in order for the intermediate-term dermal MOE to exceed 100 for airblast applicators in enclosed cabs and wearing chemical-resistant gloves, the number of acres treated would have to be no more than 10 at the maximum label rate, or 20 at one-half the maximum label rate.

- Area treated per day for the various application methods and equipment are standard values routinely used by HED. The number of acres that can be treated in an 8-hour are considered typical to high-end values.

- Body weight is the standard 70 kg value for adults, which is routinely used by the Agency. This is identified in the Exposure Factors Handbook as the mean body weight for both sexes of adults in all age groups combined, rounded to one significant figure.

- The relatively high exposures for tree bark painting

compared with other scenarios, such as airblast application, reflect the relatively high magnitude of the unit exposure (mg per lb ai handled) in PHED for this scenario. The PHED scenario for painting was based on a fungicide applied at an average rate of 0.0510 lb ai per replicate. Extrapolating the monitored scenario of 0.0510 lb ai to the oxydemeton-methyl rate of 2.0 lb ai (max), the linear relationship assumed between exposure and lb ai handled may overestimate the risk.

- Although dermal exposures during application with handheld equipment such as a high pressure handwand, backpack sprayer, or low pressure handwand were assessed using PHED data which are graded “low quality,” these data are the best currently available.

Data Gaps in Both Dermal and Inhalation Assessments. Dermal and inhalation risks could not be quantitatively assessed for two exposure scenarios because there are no appropriate chemical-specific or PHED data sets available. Also, reliable information for area treated or amount handled is unavailable. These scenarios are:

(9) applications for tree injection (ready-to-use liquids), and
(10) mixing/loading/applying liquids using soil injection.

Applications for tree injection involve placing a sealed capsule containing oxydemeton-methyl into a pressurized injector unit which is installed in holes pre-drilled into the base of trees at the root flare. Handler exposure during product mixing/loading is not expected and applicator exposure is believed to be minimal.

Soil injection uses (shade, nursery trees and shrubs) potentially involve mixing, loading, and applicator exposures. Oxydemeton-methyl is mixed and loaded into an injection devise and injected six inches below the soil surface at the drip line. There are no PHED data sets sufficiently representative of this exposure scenario for a high quality, high confidence exposure assessment. However, based on screening-level estimates using limited information on this scenario, there are significant exposure and potential risk concerns for the soil injection, primarily associated with mixing/loading activities. The data necessary to assess these risks include: exposure data, the typical number of trees treated daily, and the typical trunk diameter of the treated trees.

Summary of Incidents Reports. HED has reviewed the OPP Incident Data System (IDS), Poison Control Centers (PCCs), the California Department of Food and Agriculture (Department of Pesticide Regulation), and the National Pesticide Telecommunications Network (NPTN) data bases for reported incident information for oxydemeton-methyl. Of the 634 cases reported to PCCs (1985-1992), the majority involved workers indirectly exposed (e.g., not handlers) to spray drift. Analysis of the PCC data indicated that exposures to oxydemeton-methyl are less likely to require medical care or result in symptoms than other cholinesterase inhibiting compounds. Of the 20 cases submitted to the California Pesticide Illness Surveillance Program (1985-1994), a total of 13 persons had systemic illnesses and the majority of these illnesses were associated with activities such as mixing/loading/applying. Overall, oxydemeton-methyl was not among the 10 highest rankings of hazard derived from California and PCC data. Measures to reduce risk to applicators and handlers of oxydemeton-methyl should be consistent with other OP's and carbamates.

4.4.3 Occupational Postapplication Exposures and Risks (Reentry Intervals)

HED has determined that there is potential exposure to persons entering treated sites following application of oxydemeton-methyl-containing products. Postapplication scenarios were classified as intermediate-term (seven days to several months) based primarily on the frequency of exposure. Workers are expected to be involved in postapplication activities such as harvesting, scouting, irrigating, etc. in various crops where exposure to oxydemeton-methyl-treated crops is likely to occur daily for one week to several months. This frequency of exposure is most likely to occur during hand harvesting of cole crops (cauliflower, broccoli, Brussels sprouts) where 51-100% of the crop is treated with oxydemeton-methyl. Only postapplication dermal exposure was assessed because postapplication inhalation exposure is expected to be negligible.

4.4.3.1 Postapplication Exposure Scenarios

The scenarios likely to result in postapplication exposure are as follows:

- harvesting low growing fruits and vegetables;
- harvesting citrus fruit and high row crops such as sweet corn;
- scouting, weeding, hoeing, and other non-harvesting activities associated with low growing crops; and
- pruning and thinning non-bearing fruit crops (including grapes) and other activities such as mechanical nut harvesting.

Current labels include a restricted-entry interval (REI) of 48 hours, or 72 hours for regions where average rainfall is less than 25 inches per year.

4.4.3.2 Data Sources and Assumptions for Postapplication Exposure Calculations

Four reentry studies (MRID 00158210 grapes; MRID's 00158208 and 00158209 cauliflower and broccoli; MRID 43821401 cauliflower, cotton, bell peppers, and sugar beets) were conducted for oxydemeton-methyl formulated as Metasystox-R (a 25% ai EC).

The HED reviews of three of the studies (MRID's 00158210, 00158208, and 00158209) concluded that they do not meet the requirements of Subdivision K and the FIFRA '88 Acceptance Criteria due to a general lack of QA/QC data. Furthermore, no indication was given concerning the method used for determining the surface area of the leaf disks (i.e., whether one or both sides of the leaf disk were taken into account).

Data from the fourth study, MRID 43821401 supplemented with climatological data (MRID 44214001), was found to be acceptable and has been used to estimate REI's for the crops tested (cotton, bell peppers, cauliflower, and sugar beets), and to bridge to other crops for which no data are available. Cotton and bell peppers were treated with the 2 lb/gal EC formulation at 0.5 lb ai/A/application applied two times at an interval of 14 days. Cauliflower and sugar beets were treated with the same formulation at 0.5 and 0.75 lb ai/A/application, respectively, applied three times at an interval of 10 to 14 days. Applications were made at the maximum registered use rate. Dislodgeable foliar residue (DFR) samples were collected from each crop at intervals from one hour to 35 days postapplication and analyzed for residues of oxydemeton-methyl and its sulfone metabolite. Climatological information indicated no rainfall occurred during the sampling period.

The results of the reported dislodgeable residues at the various sampling intervals are presented in **Table 8**. In some cases, the sampling intervals were not carried out long enough to yield MOE's that exceed 100. Therefore, a linear regression analysis, using the natural logarithm of the residues versus the postapplication interval, was conducted for each of the four crops. The results of these analyses, presented in **Table 9**, were used to predict DFRs for each of the crops tested. The predicted DFR results for these crops were also used for extrapolation, where possible, to corresponding general crop groups. Thus, cauliflower DFR data were considered representative of other cole crops; bell pepper DFR data were considered representative of eggplant; and cotton and sugar beet data were assumed to represent those crops only.

It is HED's general policy to estimate REI's for crops for which no chemical-specific data are available by assuming that the initial DFR is 20 percent of the applied amount, and that the dissipation rate is 10 percent per day. Standard residue transfer values (transfer coefficients) that are unique for various tasks and activities associated with general crop groups are also utilized for postapplication risk assessment. However, in the case of oxydemeton-methyl, REI's for crops that could not be represented by the categories mentioned above (e.g., corn, grapes, non-bearing fruit trees), were estimated using a surrogate, range-finding analysis based on existing DFR data. This analysis utilized the regression-predicted, zero-day DFR values for cauliflower, cotton, bell peppers, and sugar beets to calculate an average percent initial DFR value (i.e., the average of the calculated initial DFRs for each crop, presented in **Table 9**). An average daily dissipation rate was also estimated based on the individual daily dissipation rates for each of the crops tested. The resulting average initial DFR was 11 percent of the applied amount for the last application, and the average dissipation rate was 21 percent per day.

Because it was difficult to predict exactly what activities (to determine the corresponding transfer coefficients) would be performed on crops other than those already categorized, a range in transfer coefficients of 1,000 cm^2/hr to 10,000 cm^2/hr was used to bracket the potential job/task activities. The results of this surrogate assessment, presented in **Table 9**, indicate that MOE's for crops/activities with low transfer coefficients (i.e., 1,000 cm^2/hr) and an application rate of 0.5 to 0.75 lb ai/A would be less than 100 and of risk concern until the 15th day after application. MOE's for crops/activities such as corn, with high transfer coefficients (i.e., 10,000 cm^2/hr) and the same application rate, would be less than 100 and of risk concern until the 25th day after application.

Table 8. Postapplication Dose and MOE for Cauliflower/Cotton/Bell Pepper/Sugar Beet Harvesters

Sampling Interval	Mean DFR (μg/cm^2)				Dermal Dose (mg/kg/day)[a]				MOE[b]			
	Cauli-flower	Cotton	Bell Pepper	Sugar Beets	Cauli-flower	Cotton	Bell Pepper	Sugar Beets	Cauli-flower	Cotton	Bell Pepper	Sugar Beets
0	0.14	0.21	0.92	3.1	0.040	0.024	0.42	0.35	7.6	12	0.71	0.85
1	0.025	0.14	0.90	2.0	0.0071	0.016	0.41	0.23	42	18	0.73	1.3
2	0.024	0.11	0.44	1.1	0.0069	0.012	0.20	0.13	44	24	1.5	2.4
5	0.011	0.017	0.32	NS	0.0031	0.0019	0.15	--	95	150	2.0	--
7	0.0065	0.012	0.27	0.76	0.0019	0.0014	0.12	0.087	160	220	2.4	3.5
14	ND	ND	0.15	1.3	--	--	0.070	0.15	--	--	4.3	2.1
21	ND	ND	0.079	0.82	--	--	0.036	0.094	--	--	8.4	3.2
28	ND	ND	0.035	0.28	--	--	0.016	0.032	--	--	19	9.4
35	ND	ND	0.027	0.095	--	--	0.012	0.011	--	--	25	28

NS = not sampled; ND = nondetected

Note: The LOQ value for cauliflower is 0.0045 μg/cm^2; for cotton the LOQ is 0.0065 μg/cm^2; and for both bell pepper and sugar beets the LOQ value is 0.010 μg/cm^2

[a]Dermal Dose (mg/kg/day) =([DFR (μg/cm^2]*[T_c (cm^2/hr)]*[1 mg/1,000 μg conversion]*[8 hr/day]/70 [Body Weight], where Tc = 2,500 cm2/hour (for cauliflower harvesting), 4,000 cm2/hour (for bell pepper harvesting), and 1,000 cm2/hour (for early season scouting of cotton and maintenance activities for sugar beets).

[b]MOE = NOAEL (0.3 mg/kg/day)/Dermal Dose (mg/kg/day); MOE of 100 is necessary.

Table 9. Predicted DFR's, Doses, and MOE's Based on Chemical-Specific Data (MRID 43821401)

Crop	cauli-	cotton	bell	sugar	**Averag**	cauliflow	cotton	bell	sugar	**Averag**	cauliflowe	cotto	bell	sugar	**Average**
App. rate lb ai/A	0.5	0.5	0.5	0.75	0.5625	0.5	0.5	0.5	0.75	0.5625	0.5	0.5	0.5	0.75	0.5625
% initial DFR[a]	1%	4%	12%	26%	11%	1%	4%	12%	26%	11%	1%	4%	12%	26%	11%
dissipation /day	30%	36%	10%	7%	21%	30%	36%	10%	7%	21%	30%	36%	10%	7%	21%
Adjusted[b] r^2	0.74	0.96	0.96	0.80	NA	0.74	0.96	0.96	0.80	NA	0.74	0.96	0.96	0.80	NA
DAT	DFR (ug/cm2)[c]					Dose (mg/kg/day)[d]					MOE[e]				
0	0.066	0.22	0.68	2.2	0.7	0.019	0.025	0.31	0.25	0.078	16	12	1.0	1.2	3.9
1	0.046	0.14	0.61	2.0	0.5	0.013	0.016	0.28	0.23	0.062	23	19	1.1	1.3	4.9
2	0.032	0.09	0.55	1.9	0.43	0.0092	0.010	0.25	0.22	0.049	32	29	1.2	1.4	6.1
3	0.023	0.06	0.50	1.7	0.34	0.0065	0.006	0.23	0.20	0.039	46	45	1.3	1.5	7.7
4	0.016	0.037	0.45	1.6	0.27	0.0045	0.004	0.21	0.18	0.031	66	70	1.5	1.6	9.7
5	0.011	0.024	0.41	1.5	0.21	0.0032	0.002	0.19	0.17	0.024	95	110	1.6	1.8	12
6	0.0078	-	0.37	1.4	0.17	0.0022	-	0.17	0.16	0.019	140	-	1.8	1.9	15
7	-	-	0.33	1.3	0.13	-	-	0.15	0.15	0.015	-	-	2.0	2.0	19
8	-	-	0.30	1.2	0.11	-	-	0.14	0.14	0.012	-	-	2.2	2.2	25
9	-	-	0.27	1.1	0.09	-	-	0.13	0.13	0.010	-	-	2.4	2.4	31
10	-	-	0.25	1.0	0.07	-	-	0.11	0.12	0.0077	-	-	2.6	2.6	39
11	-	-	0.22	1.0	0.05	-	-	0.10	0.11	0.0061	-	-	2.9	2.8	49
12	-	-	0.20	0.9	0.042	-	-	0.093	0.10	0.0048	-	-	3.2	3.0	62
13	-	-	0.18	0.8	0.034	-	-	0.084	0.093	0.0038	-	-	3.6	3.2	78
14	-	-	0.17	0.8	0.027	-	-	0.076	0.087	0.0031	-	-	4.0	3.5	98
15	-	-	0.15	0.7	0.021	-	-	0.069	0.080	0.0024	-	-	4.4	3.7	120
24	-	-	0.061	0.36	0.0026	-	-	0.028	0.041	0.0003	-	-	11	7.4	990
25	-	-	0.055	0.33	0.0021	-	-	0.025	0.038	0.0002	-	-	12	8.0	1300
46	-	-	0.006	0.067	-	-	-	0.0031	0.007	-	-	-	98	39	-
47	-	-	0.006	0.061	-	-	-	0.0028	0.007	-	-	-	110	42	-
59	-	-	-	0.025	-	-	-	-	0.002	-	-	-	-	100	-

Notes for Table 9:

[a]Percent initial DFR was based on the predicted day zero value divided by the final application amount; two applications of 0.5 lb ai/A to cotton and bell peppers at 14-day intervals, and three applications of 0.5 and 0.75 lb ai/A to cauliflower and sugar beets, respectively, at 10- to 14-day intervals.

[b]Adjusted r-squared for first order linear regression based on detected values only.

[c]The predicted DFR values presented are based on one-half of the values reported in the study, because the reported results were calculated based on single-sided samples (i.e., the surface area of one side of the leaf, rather than both sides, was used in the calculation).

[d]The Doses were calculated using the following Tc: 2,500cm2/hr (cauliflower), 4,000 cm2/hr (bell peppers), and 1,000 cm2/hr (cotton, sugar beets, and "Average").

[e]MOE's for the "Average" column are based on a low-contact transfer coefficient (1,000 cm2/hr). If a high-contact transfer coefficient (10,000 cm2/hr) were used, MOE's would be one order of magnitude lower.

The following additional assumptions and factors were used to complete the postapplication exposure assessment:

- Standard transfer coefficients (Tc) of 2,500 cm^2/hr for cauliflower, 4,000 cm^2/hr for bell peppers representing routine crop-production tasks such as scouting, hoeing, thinning, irrigating and harvesting activities, and 1,000 cm^2/hr for early season cotton scouting and 4,000 cm^2/hr for late season cotton scouting.
- Average work day interval represents an 8-hour workday and the average body weight of an adult postapplication worker is 70 kg.
- DFR values reported in MRID 43821401 have been adjusted to reflect the surface area of two leaf surfaces.

4.4.3.3 Occupational Postapplication Risk Characterization

MOE's for various REI's were derived by a comparison of dermal exposure estimates against a NOAEL of 0.3 mg/kg/day for intermediate-term exposure. The intermediate-term NOAEL was from a dermal toxicity study in the rat. An MOE $\geq$100 is generally considered to be less than HED's level of risk concern for postapplication exposure to oxydemeton-methyl.

The results of the postapplication assessment indicate that MOE's for cauliflower and other cole crops are greater than 100 on day six after the final application. For bell peppers and eggplant, MOE's are greater than 100 on day 47 after the last application. The estimated exposures for cotton and sugar beet reentry activities yielded MOE's greater than 100 no sooner than day five and 59, respectively, after the last application. Please note that for cotton, MOE's are based on a transfer coefficient of 1,000 cm^2/hr, which is reflects an early-season scouting scenario. For late-season scouting of cotton, a transfer coefficient of 4,000 cm^2/hr should be used, indicating a postapplication entry restriction foreight days to achieve an MOE greater than 100.

Many crops were not represented by the available and acceptable DFR data. For those crops, a surrogate assessment was conducted in which the remaining crops were categorized by the agricultural activities associated with them. In this assessment, MOE's for crops/activities with very low transfer coefficients (i.e., 1,000 cm^2/hr - group 1) and an application rate of 0.5 to 0.75 lb ai/A are less than 100 until the 15th day after application. Crops/activities that are expected to have primarily low (2,500 cm^2/hr - group 2) or medium (4,000 cm^2/hr - group 3) potential for dermal transfer necessitated corresponding intervals of 19 days or 21 days, respectively, to achieve MOE's grater than 100. MOE's for crops/activities with high transfer coefficients (i.e., 10,000 cm^2/hr - group 4) are less than 100 until 25 days after application. These four groupings, dependant on estimated transfer coefficient, are presented along with cauliflower, cotton, bell pepper, and sugar beets in **Table 10** below.

Table 10. Summary of Postapplication Exposure and Risk Estimates

Crop[a]	Rate (lb ai/A)	Current Max. Applic. Rate (lb ai/A)	No. of Applic. Per season	Applic. Interval (days)	Transfer coefficient cm^2/hr	MOE	Current REI
Cauliflower	0.5	0.5	3	NS	2,500	>100 day 6	The current REI is 48 hours. However, if there is less than 25 in of rain/year, the REI is increased to 72 hours
Cotton	0.5	0.75	2	NS	1,000	>100 day 5	
Bell Pepper	0.5	0.5	2 (3 for eggplant)	NS	4,000	>100 day 47	
Sugar beet	0.75	0.75	2	NS	1,000	>100 day 59	
Grouping 1[b]	0.5 - 0.75	0.5 - 0.75	2 - 3	NS 10-14 (mint)	1,000	>100 day 15	
Grouping 2[c]	0.5 - 0.75	0.5 - 0.75	2 - 3	NS	2,500	>100 day 19	
Grouping 3[d]	0.5 - 0.75	0.5	2 - 3	NS	4,000	>100 day 21	
Grouping 4[e]	0.5 - 0.75	0.375 - 075	1 - 3	NS	10,000	>100 day 25	

[a]Cauliflower DFR data are considered representative of other cole crops; bell pepper DFR data are considered representative of eggplant; cotton and sugar beet DFR data were not specifically translated to other crops.

[b]Group 1 crop/activities are:
- irrigating alfalfa, broccoli, brussels sprouts, cabbage, cauliflower, clover, lettuce, and mint

[c]Group 2 crop/activities are:
- sorting and packing ornamentals and turnips
- hand harvesting alfalfa, broccoli, brussels sprouts, cabbage, cauliflower, lettuce, and mint

[d]Group 3 crop/activities are:
- hand harvesting (also stake/tie or irrigating) beans, cucumber, melon, and musk melon, pumpkin, squash (summer and winter), and strawberries
- stake/tie or irrigating corn
- irrigating grapes or ornamentals

[e]Group 4 crop/activities are:
- all activities (such as harvest, prune, summer shake, rake, pole and pickup, and prop) for the following trees: apple, apricot, cherry, crab apple, filbert, grapefruit, grape (vine), lemon, nectarine, orange, peach, plum, prune, quince, and walnut
- hand harvesting corn or turnips
- transplanting or ball/burlaping ornamentals

Discussion of Postapplication Risk Estimates

Two main variables are used in the calculations for postapplication exposure: DFR and the residue transfer coefficient. The relative value of each of these parameters is described below:

- Chemical-specific DFR data were used to complete this assessment. These data, used to estimate REI's, have undergone review and have been considered acceptable by the Agency. However, data were not available for all crops; therefore, the existing data were extrapolated to other crops by using an average, rather than a bounding or standard maximum value. Using the average value, initial residue levels and dissipation rates were used to estimate surrogate DFRs for other crops.

- Transfer coefficients used to calculate postapplication risks are based on best professional judgment due to lack of data specific to each crop/activity combination. These transfer coefficients are the default transfer coefficients recommended by the Science Advisory Council for Exposure (Draft Policy.003, May 7, 1998). Please note the recommended transfer coefficient for grape harvesting is 15,000 cm^2/hr, as opposed to the maximum of 10,000 cm^2/hr used in the surrogate assessment.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

5.1 Acute Aggregate Risk

Acute aggregate risk estimates do not exceed HED's level of concern. The aggregate acute dietary risk estimates include exposure to oxydemeton-methyl residues in food and water. Exposure (food only) to combined resides of oxydemeton-methyl and its sulfone metabolite, based on a highly refined Tier 3 probabilistic analysis, represents 7.1% of the acute PAD at the 99th percentile of exposure for the most highly exposed population subgroup (females 13+/nursing). Exposure to all other groups represents less than 6.4% of the acute PAD. Using conservative screening-level models, the estimated maximum peak concentration of oxydemeton-methyl and its sulfone metabolite in surface water is 11.7 ppb. This estimated peak concentration is less than HED's drinking water level of comparison for exposure to oxydemeton-methyl in drinking water as a contribution to aggregate acute dietary risk. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from acute dietary exposure to oxydemeton-methyl.

5.2 Chronic (Non-Cancer) Aggregate Risk

Chronic (non-cancer) aggregate risk estimates do not exceed HED's level of concern. The aggregate chronic dietary risk estimates include exposure to oxydemeton-methyl residues in food and water. No chronic residential use scenarios were identified. Exposure (food only) to residues of oxydemeton-methyl and its sulfone metabolite, based on a Tier 3 highly refined deterministic analysis, represents 5.3% of the chronic PAD for the most highly exposed population subgroup (non-nursing infants). Exposure for the general U.S. population and all other subgroups represents less than 4.5% of the chronic PAD. Using conservative screening-level models, the estimated maximum annual average of oxydemeton-methyl and its sulfone metabolite in surface water is 0.6 ppb. This estimated average concentration is less than HED's drinking water level of comparison for exposure to oxydemeton-methyl in drinking water as a contribution to aggregate chronic dietary risk. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from chronic dietary exposure to oxydemeton-methyl.

6.0 ENDOCRINE EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed three years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of oxydemeton-methyl for endocrine effects.

7.0 CUMULATIVE EXPOSURE AND RISK

It has been determined that the organophosphates (OP's) share a common mechanism of toxicity: the inhibition of cholinesterase levels. As required by FQPA, a cumulative assessment will need to be conducted to evaluate the risk from food, water and non-occupational exposure resulting from all uses of OP's. Currently, the Agency is developing the draft methodology needed to conduct such an assessment with guidance/advice provided by the Science Advisory Panel. It is anticipated that this draft methodology will be available for comment and scientific review in 1999. Consequently, the risks summarized in this document are only for oxydemeton-methyl.

8.0 DATA NEEDS

Additional data requirements have been identified in the attached Science Chapters and are summarized here.

Toxicology Data for OPPTS Guidelines:

- No additional data are needed to satisfy standard Subdivision F Guideline requirements. Although there was a decision not to require a developmental neurotoxicity study for oxydemeton-methyl in conjunction with this RED, the Agency has recently issued a Data Call-In notice (FR42945, August 6, 1999) requiring registrants of neurotoxic pesticides to conduct acute, subchronic, and developmental neurotoxicity studies and submit the results to EPA. This Data Call-In is applicable to oxydemeton-methyl.

Product and Residue Chemistry Data for OPPTS Guidelines:

The existing product and residue chemistry data base for oxydemeton-methyl is substantially complete. These data are sufficient to reassess most tolerances and to conduct a reliable dietary (food source) risk assessment. Although a number of guideline requirements have been satisfied since the completion of the Product and Residue Chemistry Chapters in 12/97, some data remain outstanding. The absence of these required data does not impinge on the Agency's conclusions regarding which uses are eligible for reregistration. The current data outstanding requirements are included below.

- 860.1200 Label amendments are required for all ODM end-use products to specify that application using aerial equipment, when allowed, should be made in a minimum of 2 gal/A, or 10 gal/A for orchard crops.

- 860.1340 The requirement for method validation data in conjunction with proposals for revised tolerances for corn forage, field corn grain, and walnuts at the revised tolerance levels is no longer outstanding. Based on HED's review of available residue field trial data, the existing tolerances for residues of oxydemeton-methyl and its sulfone metabolite in walnuts (0.3 ppm), corn grain (0.5 ppm) , and corn forage/fodder (3 ppm), have been reassessed at lower levels of 0.05 ppm, 0.05 ppm, and 1 ppm, respectively. Although HED has previously required additional method validation data for these commodities showing recovery of residues of concern from samples fortified at the reassessed tolerance levels, Gowan has indicated (letter dated November 27, 1998) it does not wish to generate the additional analytical data necessary to support these lower tolerances.

- 860.1380 Sample storage intervals and conditions for all residue data submitted in support of tolerances must be supplied. In addition, storage stability data are needed for processed commodities and livestock commodities.

- 860.1500 Additional field trial data depicting residues of ODM and ODMS in/on **sweet corn** are required to provide both adequate geographic representation and a greater number of results by which to judge possible variability.

No field trial data are available for **sorghum stover**. Geographically representative field trial data reflecting the maximum registered application rate must be submitted for sorghum stover before the reregistration requirements for magnitude of the residue in/on sorghum stover can be considered fulfilled.

Additional field trial data depicting residues of ODM and ODMS in/on **alfalfa forage and hay** are required to provide adequate geographic representation. In addition, because there is a registered use for ODM on alfalfa grown for seed, data are required for alfalfa seed. *Due to the economic importance of alfalfa hay as an animal feed, the Agency does not consider Section 3 label restrictions against using the treated alfalfa commodities as food/feed to be practical. The current ODM Section 3 label (EPA Reg. No.10163-220) indicates that Gowan intends nation wide use for this product. In order for the Agency to consider use of ODM on alfalfa grown for seed a non-food use, the registrant would have to restrict the use of ODM to those states in which the Agency has determined that alfalfa grown for seed can be classified as a non-food use (i.e., Washington, Idaho, and Oregon) and this restriction should appear on the Section 3 label. Otherwise, the Agency must treat this use as a food use and require residue data to support tolerances for residues of ODM in or on alfalfa forage, alfalfa hay, and alfalfa seed.*

No additional data are required for **cottonseed**. In lieu of conducting additional field trials depicting ODM residues of concern in/on cotton harvested 14 days following the last of three foliar applications at 0.5 lb ai/A, the registrant intends to amend the 2 lb/gal EC (EPA Reg. No. 10163-220) product label to allow only two applications per season at 0.5 lb ai/A. In addition, the registrant must remove the restriction against the grazing or feeding gin trash to dairy or meat animals from the product label; the Agency considers such restrictions to be impractical.

The Agency currently recognizes **cotton gin byproducts** (commonly called gin trash which include the plant residues from ginning cotton consisting of burrs, leaves, stems, lint, immature seeds, and sand and/or dirt) as a RAC (Table 1, OPPTS 860.1000). Data depicting the magnitude of ODM residues of concern in/on cotton gin byproducts following application(s) of a representative formulation according to the maximum registered use patterns are required. Cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue for the ginning process. A minimum of three field trials for each type of harvesting (stripper and mechanical picker) are required, for a total of six field trials. An appropriate tolerance for this RAC should be proposed once acceptable data have been submitted and evaluated.

Occupational Exposure Data for OPPTS Guidelines

- The need for additional data will be determined when HED and the Special Review and Reregistration Division consider risk mitigation/regulatory options.